Volume XVIII NUMBER 7

This Issue in Two Section
SECTION 1

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DISEASES *of the* NERVOUS SYSTEM

A Practical Journal on Psychiatry and Neurology

JULY
1957

(Contents on Page 242)

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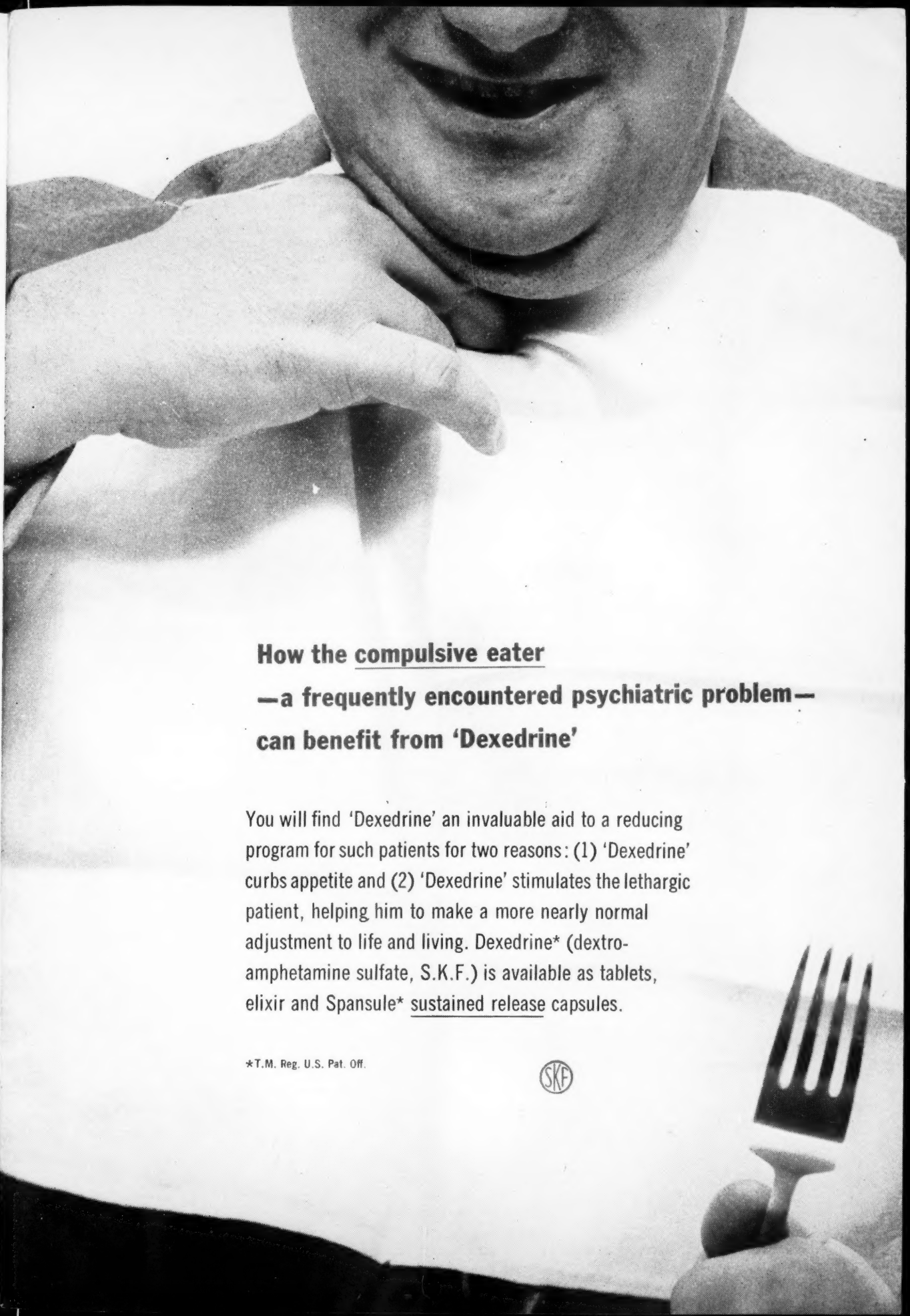

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DISEASES *of the* Nervous System

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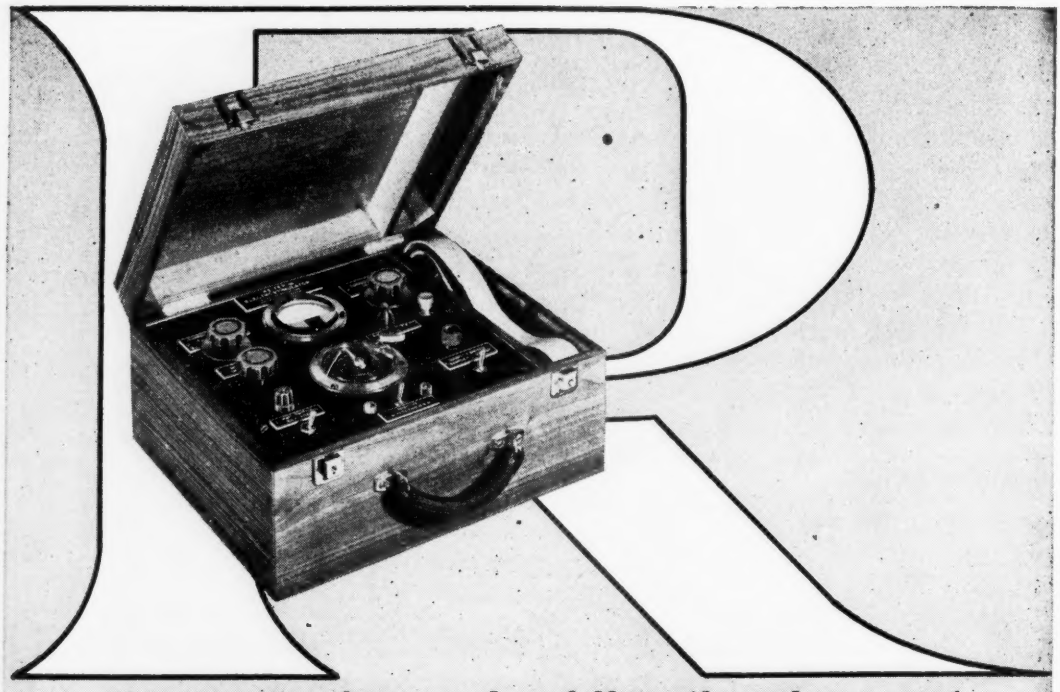

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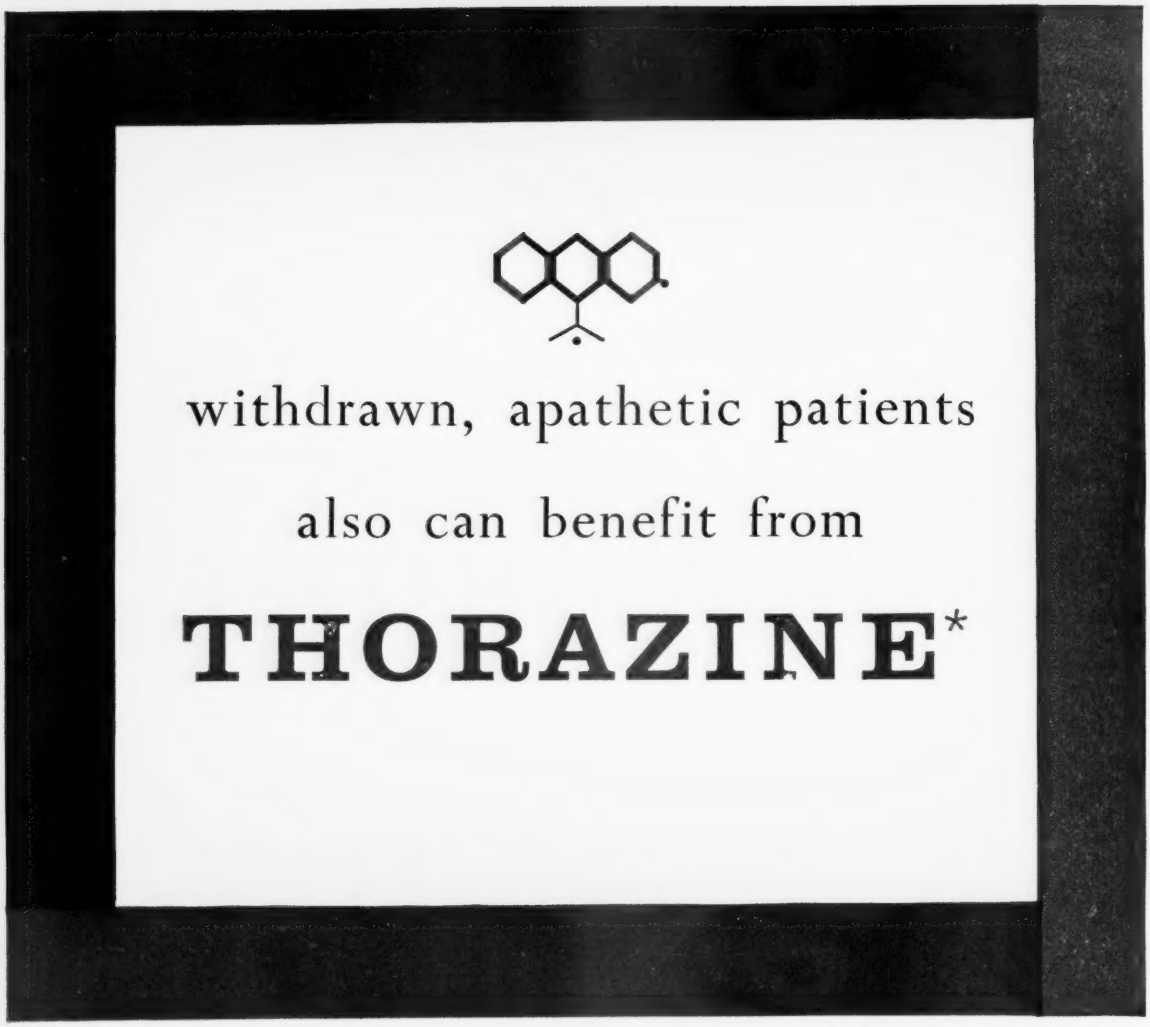

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DISEASES *of the* Nervous System

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

The Physician in the Role of Psychotherapist

EUGENE ZISKIND, M.D.

A psychotherapeutic role for the physician is the logical outcome of increased recognition accorded psychologic factors in medical illness. Because of modern sophistication in these matters a curriculum that will prepare physicians for psychotherapy need not be discussed here in detail. This has been done in a way in my book on "Psychophysiologic Medicine," in which the subject matter was presented in two parts: 1) a manual of knowledge to be acquired in psychopathology in diagnostic and therapeutic techniques, and 2) materials for orientation in the specialized literature of the psychiatrist. The curricula of most medical schools in this country now contain courses in normal development and psychopathology and therapy —often under the heading of Basic Psychiatry. These are calculated to equip all physicians for the care of psychosomatic aspects of illness, in contradistinction to Special Psychiatry for the specialist. In this presentation, therefore, consideration of training which may serve as a jumping off place for discussion of some practical aspects of the physician's role in psychotherapy will be referred to briefly with the aid of tables.

Matters of Curriculum and Training

Table 1 represents an attempt to isolate basic factors in psychopathology which would be acceptable to all psychiatrists, irrespective of their varying frames of reference.

TABLE 1—BASIC PRINCIPLES OF PSYCHOPATHOLOGY

1. *Tensions from unresolved conflict* from the core of psychopathology.
2. Major conflicts occur between *needs* of the individual and *restrictions* of his environment.
3. Resultant behavior is related to the balance between the *adaptive capacity* and the *intensity of the stress.*
4. Causative factors may be *precipitating* (e.g. current situational stresses) and *predisposing* (e.g. neurotic character patterns).
5. *Symptom formation* results from unresolved conflictual tensions.

Table 2 points up modifications in the headings of the routine medical history designed to indicate the necessary inclusion of psychological data.

TABLE 2—MEDICAL HISTORY

Verbatim recording of initial statement.
("What brings you here?")
Spontaneous description of illness.
(Often disease.)
Onset and setting of illness.
("What was going on in your life at the time?")
Presenting symptoms and their course.
Systemic (including psychobiologic) inquiry.
Past illness.
Family illness.
("What effect did it have on your life?")

Table 3 is an outline of the Life History, a new diagnostic technique for the physician, which presents the developmental history more or less chronologically but divided into major areas of life adjustment.

TABLE 3—LIFE HISTORY

Birth and infancy
Family
Schooling
Occupation
Law enforcement
Military
Sex and marriage
Religion and life philosophy
Recreation and social life
Personality traits
Current experiences

The first of several tables on therapy (Table 4) calls attention to the interpretation of the illness to the patient, showing how this important function is frequently mishandled.

From University of Southern California School of Medicine, Los Angeles, Cal.

Read at Academy of Psychosomatic Medicine, New York City, Oct. 5, 1956.

TABLE 4—INTERPRETATION OF PSYCHOGENIC ILLNESS

1. Avoidance of interpretation
2. Inadequate interpretation
3. Stigmatizing interpretation

The reasons why "Physicians Avoid Interpretation" are seen in Table 5. Obviously these are not adequate reasons even though on occasion one or more may be justified.

TABLE 5—PHYSICIANS AVOID INTERPRETATION

1. Fear of wrong diagnosis
2. Time not available
3. Fear of losing patient
4. Lack of ability
   ("causing more harm than good")

The "Results of Inadequate Interpretation" (Table 6) are sufficiently disastrous to warrant the reorientation we are now advocating. Ways for overcoming the shortcomings are easy to envisage and are a matter of training.

TABLE 6—RESULTS OF INADEQUATE INTERPRETATION

1. Chronic invalidism of patient
2. Iatrogenic disease
3. Strain on physicians
4. Disorganization of family
5. Lag in social progress

Modification of routine therapeutic procedures calls for special knowledge of "The Patient-Physician Relationship" (Table 7). This highlights the fact that secondary needs of either party or both may exist which if unrecognized and not corrected may result in the failure of therapy.

TABLE 7—THE PATIENT-PHYSICIAN RELATIONSHIP

Patient	Physician
EXCESSIVE NEEDS FOR:	
Dependency	Perfection
Acceptance	
Success, prestige	Acceptance
Authority rejection	
Guilt, masochism	Authoritative
Withdrawal	status

Basic to the considerations that are to follow is the differentiation of the goals of psychotherapy of the physician from those of the psychiatrist. The current stress is the focus of therapy for the nonpsychiatrist physician. If one sets up a series of goals of psychotherapy (as in Table 8) then the first two may be said to characterize primarily the psychotherapy of the physician; the last two psychotherapy by the psychiatrist. For simplicity of expression the former might be designated as situational therapy and the latter as character therapy. Actually no dichotomy is implied. The psychiatrist in his therapy may include all the goals, and the physician, though placing major emphasis on situational stresses, will frequently be aware of habituated attitudes and at times be able to influence them.

TABLE 8—GOALS OF PSYCHOTHERAPY

1. Acceptance of psychogenicity on authority.
2. Uncovering and working through of current stresses.
3. Uncovering and working through of neurotic character patterns.
4. Uncovering and working through of specific childhood traumata.

In general if one accepts the thesis that individuals tend to maintain a psychic equilibrium, then one witnesses a continuing adaptation in which decompensation occurs at times in varying degrees. For the milder decompensations a flexible therapeutic approach by the physician varying from the simplest to the more complex measures may be very efficacious. For deeper decompensations a formal course of psychotherapy usually includes uncovering and working through (Table 9).

TABLE 9—COURSE OF PSYCHOTHERAPY

CONSISTS OF

1. Uncovering process.
2. Working through process.

THESE INVOLVE

1. Overcoming resistance.
2. Corrective emotional experience.

At times all that is needed is a "mild boost" (Table 10).

TABLE 10—FLEXIBLE THERAPEUTIC APPROACH

1. "Boost"
   (from non-specific processes common to psychotherapy).
   Uncovering or working through may not be necessary.
2. Minimal interpretation of psychogenesis.
3. Uncovering and working through
   a. of situational stresses;
   b. of neurotic character patterns.

The non-specific psychotherapeutic processes shown in Table 11 may be sufficient to restore the decompensated equilibrium.

TABLE 11—PROCESSES COMMON TO ALL PSYCHOTHERAPY

1. Establishment of rapport.
2. Ventilation.
3. Desensitization.
4. Suggestion.
5. Education.
6. Rehabilitation.

For therapeutic purposes there is a difference in emphasis between the physician and the psychiatrist. The non-psychiatrist physician is more frequently concerned with the stresses of the present than those of the developmental past, with the external circumstances (the "situation") rather than the internal (intrapsychic) conflicts, and with the conscious and near conscious rather than the unconscious experiences. There is a greater clarity of the material of the physician as compared with that of the psychiatrist. That which is current, conscious and external is often obvious; that which is from the distant past, intrapsychic and unconscious is often obscure. The former tends to be factual, the latter hypothetical. In fact it was to fill the gaps in knowledge concerning inner behavior, unconscious behavior and remote behavioral factors that psychiatrists developed different psychodynamic systems (Freudian, Jungian, Adlerian, etc.). Each claims a system of doctrines purporting exclusive specificity of motivation for normal and abnormal behavior. Their explorations of unconscious motivations and characterological and attitudinal development, so necessary for the psychiatrist's goals, are controversial and far less important and often unnecessary for the goals of the physician.

Lest the physician feel that his therapy is superficial, hence less worthy than that of the psychiatrist, it might be well to observe the following:

First, the physician will have more success in reaching his goals since situational amelioration, control or correction are more frequently attainable than character or personality reconstruction.

Second, in many individuals in relatively good psychic balance, therapy for the situation may be all that is necessary to restore equilibrium. Bringing back a balance quickly may prevent the onset of a vicious circle leading to future chronic disorganization.

Third, even for large numbers of chronic neurotics (many of whom are incurable), situational therapy at periods of major decompensation may be the maximum that can be accomplished.

For these three reasons the physician is entitled to the attitude that there is an area of psychotherapy, that of situational therapy, in which he is king of his domain. He and he alone, if adequately prepared, can do the job better than anyone else. Certainly the psychiatrist cannot operate in this area as effectively unless he becomes a medical practitioner. Situational therapy with the physician at the helm has a potential status all of its own, as worthy as the intrapsychic therapy of the psychiatrist.

This leads to the important conclusions in Table 12.

TABLE 12—REQUIREMENTS FOR NON-PSYCHIATRIC PHYSICIAN

1. Acceptance of responsibility.
2. Acquisition of training.

The physician's role in the prevention of psychosomatic invalidism is particularly appropriate for he is the one among all the mental health workers who can exert the greatest influence.[1] This is indicated in Table 13.

TABLE 13—PREVENTION OF PSYCHOSOMATIC INVALIDISM BY NON-PSYCHIATRIST PHYSICIAN

1. Patients seen in early stages.
2. Patients beseech help.
3. All people seen by doctors.
4. No special mental health funds necessary.

The "Acquisition of Training" for psychotherapy can be obtained in three different ways (Table 14).

TABLE 14—ACQUISITION OF TRAINING

1. Experience under supervision (preceptor-preceptee training)
2. Interchange of experiences with colleague (Whitehorn).[2]
3. Post-graduate course.

Actual experience under supervision is the preferred training.

Having discussed these fundamental aspects of the physician's role in psychotherapy I would now like to consider three aids to routine incorporation of psychosomatic concepts into medical practice.

Eclecticism for the Physician

Divergence of theories and practices among psychiatrists is one of the major factors hampering the integration of psychiatric principles into medical practice. The claims of each of the psychiatric schools (the Freudians, Jungians, etc.) for exclusive specificity is very confusing to physicians. Nonpsychiatrists feel constrained to ally themselves with the philosophies and practices of one of the schools; an aping which frequently leads to "wild" or amateur psychiatry. Full utilization of the dicta of any one of the systems demands specialization in that school. On the other hand, in the absence of specialization, the physician is often likely to feel that he is performing a perfunctory, superficial service and he may shy away from it because of the low value he places on it.

Actually the physician can achieve his goals, largely by-passing schools of exclusive specificity. The point is that even though his situational therapy runs into problems of the unknown, and the physician cannot totally ignore the offered hypotheses concerning personality development, he still has lesser need for these hypotheses than the psychiatrist. When he must theorize he would do better to utilize an eclectic rather than a system orientation.

The term eclecticism has many connotations and is in general poorly understood. It is not to be equated with an attitude of dilettantism in which the therapist utilizes various concepts and techniques from different disciplines in a trial and error manner without critical evaluation. Eclectic is defined in Webster's dictionary as

"choosing what is thought best in doctrines, opinions, etc., from various sources or systems." "Ecleticism, like syncretism and skepticism, characteristically appears where several powerful antagonistic systems are in the field. Unlike skepticism, it does not doubt all systems because of the antagonistic reasonableness of each, and unlike syncreticism, it does not modify all for the sake of mutual consistency; rather it selects from each such doctrines as are satisfying . . ."

Elsewhere I have indicated that the eclectic psychiatrist,[3] not totally accepting any system of behavioral concepts on the ground that knowledge of human motivation has not yet progressed to the point of a reliable system, feels free to choose whatever doctrines he finds most adequate for the problems of his patient. In fact he contends that by so doing he creates less artefacts than by trying to fit all of his clinical problems into the framework of any one of the systematized schools, e.g., Freudian, the Adlerian, etc. To quote a statement of Stainbrook's used in another context,[4] "The essence of all these etiological constructions was not that they were all wrong, but that they were all proposed as exclusively right." The eclectic is inclined to feel that the founders of these behavioral creeds have isolated some truths, some astute clinical observations, each reminiscent of the blind man's description of the elephant. He prefers to feel free to select and utilize these independently of other system commitments.

This orientation is akin to the eclectic viewpoint which obtains so widely in medical practice. The physician accepts no overall explanation or system for all clinical entities but he weighs the evidence, clinical and experimental, for the conflicting etiologic and therapeutic concepts. The physician therefore has a kinship to the eclectic view in psychiatry and should find it congenial to his clinical thinking.

Socio-cultural Vista

The viewpoint and contributions of the social sciences buttress the position of the physician in psychotherapy. Although the research frontiers of psychiatry are reaching into the area of socio-cultural influences on behavior and psychiatrists await scientific evaluation of socio-cultural influences upon psychopathology, the general practitioner is close to these factors of social reality.

The heritage of the modern physician derives from the old family doctor who in his pursuit of the art of medicine intuitively exploited the social relations of his patients. He knew them and their environments personally and he utilized such knowledge in dealing with their maladies. The physician still attempts to reach such an understanding of his patients.

Although the practitioner is not schooled in the social sciences, he is nevertheless well versed in the folkways and mores and the social institutions of his time and place. Common sense inconsistencies in these areas are manifest to him. Once a physician recognizes his responsibility to aid a patient in confronting life situations, he is readily aware of many problems pertinent to illness. Problems related to marital felicity, satisfaction on the job, difficulties with one's children, fall into the category of current stresses in regard to which the general practitioner can bring to bear the benefits of psychotherapy. Counseling on these situations is helpful to his patients. Work at this level has the merit of relieving current stresses.

Concern for the socio-cultural factors in illness tends to avoid many of the hypothetical and controversial issues involved in specialized psychiatric therapy. It tends to shift emphasis from the early genetic, the intrapsychic and the unconscious to the current, conscious, external (situational) experiences that are the peculiar province of the physician.

Although there is need for considerable refinement and definition of the psychosocial in regard to medical problems, following are some statements that may be of interest to the clinician.

Burling[5] views "the reactions of personality organization and the patterns of social life as two aspects of an organic whole." "'. . . every maladjustment, whether we choose to call it individual or social, is a maladjustment of the same thing, the total pattern which includes both the man and his segment of society." Although both are involved in maladjustment, personal or social disorganization may be primary. It is manifestly cheaper to concentrate effort on modifying the intrapsychic element of the pattern than to spend much effort in the larger patterns of which this is a part. When this is not possible something may be gained by approaching the social part. When the social disorganization is primary, this should first be altered; but in society this may not be possible and the intrapsychic may still need to be treated. Our problem is that much of the part contributed by "sick" society is not thoroughly appreciated. Nevertheless treating the total pattern—which includes both man and his segment of society "may be necessary."

Stainbrook's[6] comments broaden the concept of psychosomatic medicine as open-ended, interrelated systems of physiology, personality, society and culture

". . . in which all can and usually do respond adaptively under conditions of stress . . . although . . . the strain can become manifest first in any of the systems." Stainbrook adds: "Since a basic conception about behavioral disease is that it represents not alone the failure of the patient but also, to a greater or less extent, the failure of the significant others with whom he was in intimate relationship, these significant others may also need help to understand how to facilitate, extend and generalize the therapeutic relearning of the patient."[7]

Glass[8] reports a shift in military psychotherapy from a patient-centered to a milieu-oriented view. Formerly therapists working back of the front lines evacuated the patient to the rear. Later psychiatrists assigned to the front lines identified emotional disturbances with the milieu interest and treated the patient locally.

Psychaitrists have at times sought to excuse their lack of interest in the patient's social orientation on the ground that the therapist must not impose his own values upon the patient. Acceptance of socio-cultural factors, however, may not involve an imposition of one's own moral code on the patient as much as a realistic consideration of the adequacy of the patient's social adjustment in what Adler called the "iron laws of co-living." Related to this failure to consider adequately the socio-cultural factor is the fact that many psychiatrists have carried on intensive therapies based entirely on the patient's statements, only to find that his biases and needs have kept the therapist from a realistic evaluation of the problem. Often this has been to the detriment of the patient, with the ironical aspect that individuals in the patient's environment might readily have supplied that which even much probing failed to uncover.

Pauline Young[9] gives some details of how social factors may affect the individual's psychic equilibrium; also how social participation may operate as a therapeutic force.

"In primary face-to-face relationships, loyalty to the group's folkways and mores is reinforced by common participation in the daily activities of the group . . . and also of strong identification, a we-feeling, with the lives and experiences of other members. . . . However, as a person's contacts widen and his activities and experiences broaden in the larger community (society), he often encounters a diversity of complex and dynamic changes and a wide variety of culture groups. The values and codes of these varied groups may be not only in sharp contrast to those of his own group, but they may frequently contradict and conflict with each other. Moreover, the various institutional codes of one's own group may not be completely integrated in a dynamic social order. The Golden Rule, for example, emphasized on Sunday may not be consonant with the weekday business contract, much less with the after-hours conduct of the sporting session. Such lack of integration may play havoc with a person's traditional modes of behavior, distort his sense of loyalty to his social heritages and present to him serious problems of conscience, and may often leave him in an anxiety ridden state.

Insight and the working through process are indispensable prerequisites to the modification of specific behavior. However, a patient's adjustment should be viewed both as a personal and a social process. That is, his practices, beliefs and attitudes to some extent must be consonant with those of his group. Furthermore, he needs to be incorporated as a functioning member in the group, if he is to gain an acceptable social role and be able to gratify adequately his wishes and needs. Through actual social participation and group relationships it is possible to gain a realistic appreciation of the scheme of social and moral imperatives.

Some persons may enter only limited activities, and only at a peripheral level. Others may need the therapist's guidance and stimulus, but once they have become incorporated into the stream of community life—will broaden their perspectives and experiences and will gradually be able to assume responsibilities and promote the general scheme of group interests and purposes.

A New Look at Medical Cost

If one asks why the psychosomatic concepts, which appear to be accepted so readily by most physicians, are not routinely applied in medical practice, a serious limitation comes to light. The reason is primarily economic.

Medical practice is organized so that physicians see 15 to 30 or more patients a day. Psychotherapeutic techniques as a rule require not less than 30 minute sessions. This means a reduction in the number of patients the physician can see each day. Correspondingly he must demand greater compensation for these sessions than for shorter visits. Even though there is an increasing acceptance of this more comprehensive type of care, not enough patients are prepared to make the greater expenditure required.

Actually the problem may not be one of increased expenditures. If our thinking is correct, there is an actual saving in the long run, although initially the expense may be greater. In a great many cases the prevention of recurrences and chronic invalidism results in a shorter course of treatment. However, this thesis remains to be demonstrated.

This demonstration is hardly likely to take place in private practice. A possible exception is the experience of a medical practitioner in our community. Dr. M. Abowitz conducted group psychotherapy once a week on 8 of his patients with gastro-intestinal problems, under the supervision of a psychiatrist. In this way the charges in hour sessions for his patients did not exceed those of their usual visits.

Those agencies, however, which have the responsibility for the long term medical care of their patients, such as veterans' facilities, medical insurance plans, and community clinics, have much to gain if the contention of savings, even in the face of initially increased costs, can be substantiated. Some of these facilities should set up pilot studies, in which a group of their patients might be treated by the comprehensive psychosomatic approach involving psychotherapy where necessary, with the other patients under the customary treatments used as controls. If not these agencies then perhaps the United

States Public Health Service or some philanthropic foundation will finance such studies. Once it can be demonstrated that there are material savings as well as enhanced health as a result of these initially more expensive methods, a great obstacle to their institution is likely to dissolve.

In conclusion I should like to repeat these observations.

1. Emphasis on situational stresses sets the stage for the physician's role in psychotherapy.

2. This role is entitled to high status because of the large number of cases for which it is indicated, the great number of potentially favorable responses and the satisfaction of performing a task which cannot be carried out as well by others.

3. The eclectic rather than system psychiatric orientation has preferential value for the physician's theorizing.

4. The physician's role in psychotherapy favors the integration of socio-cultural influences on behavior along with the psychological.

5. The financial dilemma of initially greater costs interferes with the universal practice of psychosomatic concepts and that may be resolved by a pilot study demonstrating actual savings in health and expense.

The role of the physician in psychotherapy is thus distinctive and distinguished—or discrete and discreet!

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Galactose Treatment of Multiple Sclerosis (A Preliminary Report)

JACK HARTSTEIN, M.D., and GEORGE A. ULETT, PH.D., M.D.

In a search for causative factors in multiple sclerosis some defect of the building blocks of the myelin sheath deserves further study. Prominent among the component substances of myelin are the cerebrosides which constitute much of the brain tissue. Some of these compounds are fairly well characterized as galacto-lipids, and their formation is known to be dependent upon an adequate supply of the sugar galactose. Further evidence that studies of such substances might be fruitful is found in the report of Cummings (1953) that a decreased cerebroside content is seen in and around the demyelinated areas of the cerebral cortex in cases of multiple sclerosis. Platt (1955), in a provocative article, suggests that demyelinating diseases of adult life may perhaps be related to a defective myelin structure laid down in infancy. He points out that in fants who are fed cow's milk may have less galactose available during the period of rapid growth and myelin formation and hence it is possible that the cerebrosides of the myelin sheath may, in such individuals, be synthesized from glucose. Sadu (1953) has produced changes in cerebroside, sphingomyelin and phospholipid in pigeon brains by feeding dextrose-rich or galactose-rich diets. The possible adverse effect of such glyco-cerebrosides upon the brain's susceptibility to demyelinization is, of course, a matter of speculation. Stadler et al. (1954), have presented the view that in some familial demyelinating diseases we may be dealing with a primary disorder of metab-

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olism that has only a secondary effect upon the central nervous system. Adams and Kubik (1952) have even postulated that some property of myelin may determine the localization of the pathology.

The postulation that multiple sclerosis may be related to a deficiency or abnormality in galactose metabolism is not incompatible with some current theories of the role of stress in the precipitation of attacks. Seidek and Hein-Sekula (1954) demonstrated, for example, that an increase in thyroxin level makes difficult the assimilation of galactose. The role of pregnancy, often debated as a precipitating cause of exacerbations gains some support from this hypothesis in terms of depleting body galactose stores through the secretion of milk by the lactating female.

In the face of such facts and theories it seemed of value to experiment with the administration of large quantities of galactose to patients with multiple sclerosis. This was done on the supposition that they possess some abnormality of galactose metabolism that interferes with the laying down of the myelin sheaths. It was reasoned that inasmuch as small amounts of galactose are already available in the alimentary canal from the lactose of the diet, either much larger doses were needed orally or the substance should be introduced directly into the blood stream.

We approach the problem of dose determination with some hesitancy as large amounts of galactose are known to produce opacity of the lens in immature rats (Day 1936). In the galactose tolerance test used for the investigation of liver functioning, amounts of 40 grams to 1 gram/kilo are used and Deuel (1936) has reported that the normal adult person is able to metabolize up to 25 grams of galactose within 12 hours. The role of vitamins and insulin in galactose assimilation became a consideration in our planning. Our original procedure was therefore to administer 100 grams of galactose daily, half orally and half intravenously together with vitamins and insulin. This treatment was given over a period of at least four weeks. Following this, attempts were made to continue the treatment by oral administration alone.

Determinations were made on blood galactose levels following both methods of administration and are to be reported later (Hartmann, et al.). Suffice it to say that oral administration appears to be less effective and hence, currently, various concentrations of galactose are being given by parenteral administration to multiple sclerotic patients in the out-patient clinic. A report is to be made here of our initial clinical observations.

Eleven patients were selected with known multiple sclerosis, with typical histories and findings and, in many instances, who had had diagnostic studies by more than one qualified neurologist. These patients ranged in age from 24 to 53 with a mean age of 43 years. There were 4 men and 7 women. All patients were hospitalized and given intravenously, daily, 1 liter of 5% galactose (50 grams in water solution to which had been added 2 cc. of Betolake, 1 ampoule of Ascorbine B and 1,000 mgms (1 cc) of Vitamin B_{12}. The rate of administration was such that it did not exceed 10 cc. per 10 lbs. of body weight per hour. Twenty-five units of regular insulin was given to each patient daily. All save one patient received, in addition, 50 grams of galactose given orally in fruit juice. Two patients who did not receive the oral galactose also did not receive insulin and were given the I. V. solution at a somewhat faster rate. The latter patients were treated in Portland, Oregon, through the kind cooperation of Drs. Robert S. Dow and Wilbur Larson.

Ten of the patients showed a significant reversal of symptoms with intravenous therapy (Table I).

Following the initial treatment phase, nine patients were continued on oral galactose alone, 50 to 100 grams daily with insulin for 70-90 days. This treatment regime was discarded because of extreme nausea and weakness.

In six patients who remained in the hospital, there has been a slow, but steady decline in function and a reversal of symptomatology although all are still somewhat better than on admission to the hospital. One patient has had further intravenous injections on three occasions each of from 5-7 days. On each occasion she has shown some improvement of symptomatology but due to

TABLE I

Patient	Age	Sex	Duration of Illness	Duration of Current Attack	Initial Evaluation	After 30 Days I. V. Galactose
A.D.	25	F	3 yrs.	18 mos.	Completely bedridden; diplopia (unable to read large print); marked bladder retention; complete obstipation; loss of temperature sensation in lower extremeties; bilateral extensor toe signs and increased deep tendon reflexes. Severely ataxic with resting tremor (cannot get out of bed, hold cigarette or sit up); difficulty in breathing.	Able to walk with minimal support; diplopia gone, can read ordinary newsprint; bladder function returned; bowel function reestablished; temperature sensation returned to lower extremities; bilateral toe signs and hyperactive deep reflexes unchanged; feeds self with ease; ataxia markedly lessened. Breathing normal; gained 12 lbs.
E.N.	48	F	8 yrs.	2 yrs.	Completely bedridden; hyperactive deep reflexes; bilateral Babinski, Oppenheim, and Chaddock signs; almost total paralysis, can only slightly move toes and fingers on right hand.	Increased function of quadriceps and extensors and flexors of wrist, fingers and toes; joint motion present in shoulder for first time; can raise right arm completely off bed and flex and extend wrist.
G.B.	25	F		4 yrs.	Completely bedridden; constant resting tremor and severe upper extremity ataxia; vision 10/200, unable to read or see wall clock; malfunction of bowel and bladder; left leg totally paralyzed.	Return of motion in left leg; some decrease in body tremor; vision improved to 20/40 (can now see wall clock and read ordinary newsprint). Return of bladder function.
E.T.	42	F	15 yrs.	20 mos.	Ataxic but can walk with support; constant tremor of head and neck; malfunction of bowel and bladder; marked intention tremor.	Can walk with support; improvement in bowel and bladder function; decrease in tremor and finger to nose ataxia.
J.K.	51	M	5 yrs.	3 yrs.	Completely bedridden; left leg completely paralyzed, right leg partially paralyzed; bilateral Babinski, ankle clonus, ataxia, unable to raise self or sit up in bed.	Able to sit up in bed; able to raise left leg; can get out of bed into wheelchair and back to bed.
J.N.	37	F	5-8 yrs.	2 yrs.	Difficult breathing; malfunction of bladder; numbness in all 4 extremities; unable to walk without crutches; bilateral extensor toe signs; no appetite; bilateral foot drop.	Breathing normal; can walk without support, numbness improved, no foot drop, strength improved (no longer takes Dexedrine) appetite returned; gained about 12 lbs. generally feels good.
E.H.	41	F	15 yrs.	3 yrs.	Positive toe signs; spotty sensory loss in legs, ataxic, difficulty walking, depressed.	Babinski reversed; sensation returns; ataxia markedly lessened, hops and walks better; feeling of general well-being; mildly euphoric.
M.K.	28	F	19 mos.	3 mos.	Completely bedridden; internuclear ophthalmoplegia; slurred speech; mild dysphagia; right leg partially paralyzed; bilateral Babinski's; ankle clonus; ataxia of both arms and great difficulty feeding herself; unable to raise self or sit in bed because of vertigo and ataxia.	A slight diminution of the ataxia of her right arm and a slight decrease in the vertigo which occurred on sitting or moving quickly in bed.
C.W.	47	M	9 yrs.	9 yrs.	Completely bedridden; unable to raise self in bed; marked adductor spasm, hyperactive deep reflexes, bilateral extensor toe signs, dissociation of conjugate vision.	Can raise head and shoulders off bed; slight decrease in ataxia.

TABLE I (Continued)

Patient	Age	Sex	Duration of Illness	Duration of Current Attack	Initial Evaluation	After 30 Days I. V. Galactose
A.F.	41	M	9 yrs.	3 yrs.	Completely bedridden; slurred speech, severe ataxia of upper extremities; inability to move lower extremities; bilateral toe signs.	Can wiggle toes, bend legs at knees and raise legs; can raise self out of wheelchair and stand holding to bed; speech improved.
D.H.	53	M	9 yrs.	2 yrs.	Completely bedridden; spastic quadriparesis with hyperactive deep tendon reflexes; bilateral toe signs.	Return of ability to open and close left hand; can raise both arms above head; some decrease in adductor spasm, feeling of pressure at back of neck gone.

lack of suitable veins for such repeated intravenous treatments, she is now being treated with small amounts (2.5 gm) of galactose (50 cc. of a 5% solution) given daily by clysis with 150 units of hyaluronidase and continues to improve. Patient E. H. received no oral galactose and her symptomatology returned within 2 weeks of discharge from the hospital and failed to again remit with I. V. administration of 25 gm. three times per week given for one month. Patient J. N. has had a vacillating course but with definite improvement and is now receiving 25 gm. galactose (100 cc. of a 25% solution) twice weekly given intravenously within a 10 minute period.

These initial observations are, of course, far from conclusive and the literature is replete with new treatments for multiple sclerosis which seemed promising only in the first report. As Schumacher (1950) has pointed out the validation of any treatment for this illness must be conducted over a period of several years. Such long term evaluation of galactose treatment is now planned, but it was hoped that a preliminary report of this work might stimulate other workers to make observations upon the method. With such reservations, however, we can state that the clinical findings suggest that a treatment regime involving administration of galactose is effective in reversing some of the symptoms of multiple sclerosis. One would suspect that only early or incomplete lesions would be most likely to reverse with such treatment. The sugar must be continually given to maintain the gains achieved. Failure to maintain improvement with oral administration, together with observation of blood galactose levels now in progress, would suggest that multiple sclerosis patients have a defect in galactose metabolism, and that such a defect may be concerned with the manner in which galactose is absorbed from the alimentary tract.

Authors' Note: Galactose was made available by Merck Chemical Company of Rahway, New Jersey and the Mallinckrodt Chemical Company of St. Louis, Missouri.

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Therapeutic Trial of Chlorpromazine In Patients With Chronic Mental Illness

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When this trial study of chlorpromazine response in patients suffering primarily from chronic mental illness was started in September 1954, there were relatively few investigations which concerned themselves with the effect of the drug on this type of patient. Since its introduction into clinical use by Delay and Deniker[5] in 1952, few drugs have shown such apparent promise in the treatment of tension states in both minor and major psychoses. The chemistry, physiology, pharmacology, animal experimentation and some clinical studies have been thoroughly summarized.[9] A recent brochure[10] dated April 1955, was concerned with the treatment of institutionalized psychiatric patients. This booklet contains 132 references to literature, although relatively few are concerned primarily with treatment of patients with chronic mental disorders. Lehmann and Hanrahan[8] were the first to use the drug clinically in America.

The mode of action of chlorpromazine seems to be more sympatholytic than parasympatholytic with inhibition of some of the central nervous system functions.[4] Its clinical effect has been described as a "chemical lobotomy." The toxicity of the drug is low. Side effects and complications usually consist of a tendency toward hypotension, drowsiness from which the patient is easily awakened, dryness of the mouth, pallor, tachyardia and palpitation, allergic skin reactions, jaundice, occasional hyperthermia to a mild degree. The rare but serious complication of agranulocytosis has recently been noted.

The dosage of drug varies with the different investigator and generally corresponds to the type of patient treated. In general, the less severe type of disorders are given smaller doses and those with more severe chronic involvements are given larger doses.

Clinical results in neuropsychiatric disorders usually show various types of improvement. Anton Stevens[1] finds that schizophrenics show a decreased reaction to delusions and hallucinations and develop a "psychic indifference." Azima and Ogle[2] treated 100 non-selected patients with psychoneurotic, schizophrenic and affective disorders and found that 75% of the neurotic states improved to a moderate degree, with return of anxiety in 70% of the cases. Improvement occurred only in those schizophrenics who were tense and excited, and a moderate degree of improvement was noted in about one-half of the affective disorders. Elkes and Elkes[6] studied 27 patients with placebos as control. Eighteen of them showed various degrees of improvements with a gain in weight. Kinross-Wright[7] found considerable improvement in delirious and toxic states to small doses of the drug intramuscularly. Manic aspects of the affective disorders showed a considerable improvement, but about half of the schizophrenics showed no substantial benefit. Winkelman[11] noticed reduction of severe anxiety, a suppression of the intensity of phobias and obsessions, tendency to reversal or modification of the paranoid type of psychosis and improvement in the manic or agitated types. Hostile, senile psychotic patients became more manageable.

Method and Scope

The treatment covered the period between September 13, 1954 and January 9, 1955 with follow-up observations until March 15, 1955. The series consisted of 50 patients consecutively receiving treatment for the first time. To reduce variables, a standard regimen of treatment was employed to establish a base of references for results. Subsequently, patients were treated according to individual

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response, and this will be incorporated in a future evaluation. Patients were selected for treatment primarily for the relief of tension, agitation, or anxiety regardless of diagnostic category.

Patients were all male; ages varied between 24 and 68 years with a mean of 37.5; years of acute illness varied between 0.5 to 35 with a mean of 9.3; years of hospitalization varied between 0.3 and 17 with a mean of 3.5; number of hospitalizations varied between 1 and 11 with a mean of 3.3.

The regimen consisted of 28 days of treatment. Initially, patients were observed and their basic behavior and mental state noted. Laboratory examinations included recent C.B.C., urinalysis, X-ray of chest, and cephalin flocculation tests. Oral medication was started at 50 mgms. three times a day and increased by 50 mgms. a day every third day until 300 mgms. daily were given as an average maximum dose. This dosage was maintained for about two weeks and in the final week patient was given 150 mgms. a day. To prevent undue complications or side effects, the patients were restricted largely to the ward for the first week and then subjected to a fairly active program involving a moderate degree of physical activity. Group and individual psychotherapy, where applicable, were given. The group was carefully observed, and frequent notes and observations made. Blood pressure, temperature, and pulse were recorded twice daily. Weight was taken once a week. After treatment was completed, evaluation was made about two weeks later by a board consisting of the two psychiatrists, the nurse, and the aide in charge of the program. The patients and records were then studied for the follow-up evaluation. If the patients were unable to take medication orally, they were given 50 mgms. intramuscularly twice daily increasing by 50 mgms. every third day as needed until given four times a day. As soon as possible, this was substituted by the oral medication. Contraindications to the treatment were serious myocarditis, liver disease or dysfunction, and anemias. Caution was used in regard to the use of barbiturates, narcotics and anesthetics, with special notation as to coramine and metrazol, which, according to literature, seem to induce convulsions. Older and more debilitated patients were given the dosage more gradually and at lower levels.

Findings

The relationship of the types of improvement to the diagnosis is listed in Table I, including definition of the degrees of improvement. The incidence of the side effects and complications is noted in Table II with reference to the type, frequency, intensity and duration. The difference between objective findings and subjective symptoms is shown in Table III. Follow-up findings are noted in Table IV and include the number of mgms. given per patient, and list the relapses in reference to the diagnosis and time occurrence after treatment ended.

TABLE I

Results of Chlorpromazine Therapy in Relation to Diagnoses

	TYPES OF IMPROVEMENT				
Disorder	**Good**	**Moderate**	**Mild**	**None**	**Total**
Schizophrenic	4	10	15	8	37
Affective	3	0	2	1	6
Psychoneurotic	3	1	0	2	6
Senile psychosis	0	1	0	0	1
Total	10	12	17	11	50

Good—Good Improvement from anxiety and/or psychoses.
Moderate—Moderate improvement from anxiety and/or psychosis; usually on open ward.
Mild—Mild improvement from anxiety and/or psychosis; usually on closed ward.

TABLE II

Side Effects Or Complications to Chlorpromazine Therapy With Intensity and Duration of Reactions.

Side Effects or Complications	**—Intensity—**			**—Duration in— Weeks**				
	Mild	**Moderate**	**Severe**	**1***	**2**	**3**	**4**	**No. of Pts**
Drowsines	15	5	0	11	4	1	4	20
G.I. disturbances	4	1	0	3	1	1	0	5
Dizziness	4	0	0	4	0	0	0	4
Diastolic BP, zero	0	0	4	4	0	0	0	4
Dermatitis	2	0	0	0	2	0	0	2
Dryness of mouth	1	0	0	1	0	0	0	1
Syncope	1	0	0	1	0	0	0	1
Hypertension	0	1	0	0	0	0	1	1
Frequency urine	0	1	0	0	0	0	1	1
Seizure	0	1	0	1	0	0	0	1
Jaundice	1	0	0	0	1	0	0	1
Total	28	9	4	25	8	2	6	41†

*Occasionally to one week.
†Including eight patients with more than one reaction.

TABLE III

Comparison of Objective to Subjective Types of Improvements

Types	IMPROVEMENTS Objective	Subjective	Difference (objective)
Good	10	10	+ 0
Moderate	13	11	+ 2
Mild	16	12	+ 4
None	11	17	+ 6
Total	50	50	+12

TABLE IV

Incidence of Relapses After Chlorpromazine Therapy

——Disorders——			RELAPSES Days After Treatment					Aver.
Schizophrenic	Affective	Senile	Total	0 - 7	14 - 21	45 - 60	75	No. Mmgs.
7	4	1	12	6	2	3	1	6100

Discussion

Thirty-nine of the 50 patients showed the various degrees of improvement (Table I) although the majority appear to be in the moderate or mild categories. Though there were not enough patients for statistical evaluation in the affective or psychoneurotic group, there appeared to be a tendency toward better improvement in these categories. The follow-up studies (Table IV) indicated a relapse in seven of the 29 improved schizophrenic, four of the six improved affective and in the single senile psychotic, types of disorder. Since 22 of the 29 patients with schizophrenic disorders maintained their improvement, this drug seems to be fairly effective in reduction of the tension states associated with affective reactivity to delusions or hallucinations. Functionally, the number of patients receiving electrotherapy had been reduced from an average of about 12 to three daily, by reason of the introduction of this type of treatment.

Since electrotherapy upsets so many patients there is a greater degree of cooperation and receptivity to this treatment rather than electrotherapy. The advantages were also noted by Bower.[3] It is noted that several of the affective disorders did much better with electrotherapy than with chlorpromazine. The side effects in this series consisted primarily of drowsiness to a mild degree primarily in the first week in most of the cases, mild G.I. disturbances including nausea, constipation and bloating, dizziness was mild and transient. The one case of syncope responded to postural treatment. Although the drug, in general, tends to have a hypotensive effect, one patient had persistent hypertension which was present before, during, and after treatment—likely as an autonomic response to his conflicts. It is interesting to note that one patient with schizophrenia developed grand mal during treatment. His last course of ECT ended in August 1953. There was no history of seizure or convulsive tendency prior to this time. EEG taken after the seizure occurred was within normal limits. The patient had no recurrence of the disorder and was getting no other medication than chlorpromazine. One patient had mild jaundice occurring about the 15th day and improved spontaneously in about two weeks. Two patients developed allergic urticarial dermatitis which subsided spontaneously in about two weeks with symptomatic medication.

During the evaluation it was noted that there appeared to be some difference between the objective evaluation of the patient and his subjective symptoms. It was found that the patient had a tendency to have a more pessimistic viewpoint of the degree to which he had improved. (Table III.) In the moderate types of improvement two patients were observed to be better than they reported. Four patients were found to be better objectively, in the mild types of improvement, than they felt subjectively. Six patients thought they were not any better but were observed to show some definite clinical improvement. The general publicity attached to the drug has indicated a considerable demand, especially on the part of the relatives and at times of the patients, to use this "miracle drug." It is noted that the relatives tend to have an exaggerated optimism to any improvement through use of this drug. The above comments point to a need for more careful evaluation of the response to chlorpromazine. This could be made in appropriate hospitals with control groups to help eliminate the factor of improvement gained by the extra attention and enthusiasm which generally accompanies a new form of treatment.

Summary

1. This study includes the results obtained from 50 patients subjected to a trial of a chlorpromazine regimen from September 13, 1954 to January 9, 1955 with a follow-up observation until March 15, 1955.

2. Patients were all male. Mean age of 37.5 years, number of years of illness 9.3, years of hospitalization 3.5, and times of hospitalization 3.3.

3. A standard regimen of treatment was given in order to determine the base of therapeutic response in patients largely suffering from chronic mental disorders.

4. The regimen consisted of a standard daily dose of medication orally, with a build-up period from one week, maximum dosage of about 300 mgms. for two weeks and a tapering-off dose of 150 mgms. a day the last week. Patients were subjected to a well-integrated total push program under constant observation and checked daily for their physiological reactions including temperature, pulse, blood pressure.

5. Evaluation made by a board about two weeks after the end of treatment.

6. The series consisted of 37 patients with schizophrenic, six with affective, six with psychoneurotic, and one with senile psychotic disorders.

7. Thirty-nine patients showed varying degrees of improvements of whom 12 relapsed in the follow-up period.

8. Types of improvement were mostly in the moderate and mild categories with persistence in 22 of the 29 schizohprenic patients.

9. Complications were mild and not disabling, consisting mostly of drowsiness, G.I. disturbances and dizziness of a mild nature.

Conclusions

1. Chlorpromazine appears to be a safe drug in treatment of neuropsychiatric disorders and seems to be of value in relieving reactive tension states regardless of diagnostic category.

2. Side effects and complications are usually mild and not serious.

Authors' Note: Chlorpromazine used in this study was supplied by Smith, Kline and French Laboratories under the trade name of Thorazine.

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Evaluation of Transorbital Lobotomy With a Control Group

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In contrast to prefrontal lobotomy,[2,6,7,10,11] controlled studies of the effects of transorbital lobotomy have been sparse.[2,3,4,5] Sytematic efforts to measure its results and to evaluate this form of psychosurgery on a long-range follow-up basis have not been reported. One consequence has been the lack of reliable and valid evidence to compare transorbital lobotomy with other modes of treatment of a similar group of psychiatric cases.

This is a report on the outcome of transorbital lobotomy upon a group of psychotic patients compared with a matched group of control patients receiving typical somatic treatment, such as EST and ICT, and followed-up one and a half years after treatment. Later reports following-up these patients for longer periods are planned.

In addition to clinical impressions, measurements were made in the hospital before and after treatment by the Malamud-Sands[1] and Wittenborn[12] rating scales, and a psychometric battery composed of the Wechsler-Bellevue I. Q., Rorschach, and Bender-Gestalt tests. Before and after returning home from the hospital, a social history, including a formalized check-list of items, and the Wittenborn rating scale of the patient's behavior at home were obtained by social caseworkers.

Patients receiving transorbital lobotomy had previously failed to respond to other modes of therapy. Permission from the patient and responsible relatives or guardians was obtained before psychosurgery was performed. At the same time, the responsible relatives were made aware of the possibility of the patient being released from the hospital soon after the operation and were urged to prepare for this eventuality. A total of 79 candidates for psychosurgery were accumulated in 1953 at one state hospital, stopping at this point to remain within the capacity of the staff to properly study them. As a result of a previous statistical analysis of a large number of patients lobotomized earlier,[8] five major factors were designated as significant on which the control cases were to be matched: diagnosis, sex, race, age and length of hospitalization. (Although age was not found to be a statistically significant prognostic factor in a prior study, this variable was nevertheless included to allow stricter control on possible intervening factors affecting outcome of treatment.)

Of this lobotomized group, 39 in-patients in another state hospital located in a different part of the state were matched on these five factors within the following limits:

1. Age: No greater difference than 9 years.
2. Sex: Identical.
3. Race (Color): Patients of the major ethnic groups, Anglo-American, Spanish-American), and Negro, were matched.
4. Diagnosis: Precisely matched, according to current A.P.A. nosology.
5. Duration of hospitalization: No greater difference than 9 months.

For purposes of the present analysis, the original two groups totaling 78 study-patients were reduced to 42, eliminating those pairs of cases where any of the measurement data was not obtained on either one of the pairs. Some of the lobotomized patients were released from the hospital before all of the rating scales and psychometric tests could be made (e.g., on weekends when the study-staff were not present or turn-over of ward personnel). Other problems of communication and coordination of compilation of the data in the two large hospitals caused a few omissions in certain parts of the data. To what precise extent our data are biased because of these factors, cannot be determined.

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Confining the results to the characteristics of the group of patients studied, however, should make inferences from these data reasonably reliable.

The average age of both the lobotomized and control groups of patients reported herein was 40 years. Each group contained 20 females and 1 male, of which 19 were white and 2 Negro. The diagnostic categories included 19 schizophrenics, divided into 10 paranoid, 5 hebephrenic, 2 catatonic and 1 mixed, and 3 manic-depressive psychotics—2 depressed and 1 manic. Average length of hospitalization for the psychosurgical group was 7 years and 5 months prior to treatment, while 7 years and 4 months was the average for the control patients. Consequently, these five characteristics are highly similar for both study-groups.

The five matched characteristics of the paired lobotomized and control patients are listed below in Table 1:

Results

Evaluation of the outcome of transorbital lobotomy was based upon four major criteria: clinical impressions, Malamud psychiatric rating scales, Wittenborn rating scales, and release from the hospital. The data from the psychometric battery were insufficient to permit a valid statistical analysis for these groups of subjects.

Clinical Impressions:

Initial evaluations of the subjects' mental status were made from five days to a month following psychosurgery. Evaluations were the consensus of the neurosurgeon, ward physicians, nurses, and attendants. Of the 21 matched lobotomy patients, 48 per cent were regarded as improved and parolable, 43 per cent improved but unparolable, 9 per cent unimproved, and none as worse. One year later, the clinical impression did not differ significantly, with 52 per cent evaluated as improved, 43 per cent as unimproved,

TABLE 1

Matched Characteristics of Transorbital Lobotomy and Control Patients

Transorbital Lobotomy Cases:					Control Cases:				
Age	Sex	Color	Diagnosis	Length of Hospitalization	Age	Sex	Color	Diagnosis	Length of Hospitalization
62	F	W	Manic-Dep., Dep. Type	6 years 4 mos.	53	F	W	Manic-Dep., Dep. Type	6 years 5 mos.
33	F	W	Schiz-Par.	1 year 3 mos.	35	F	W	Schiz.-Par.	1 year 4 mos.
52	F	W	Schiz.-Par.	19 years	52	F	W	Schiz.-Par.	18 years 7 mos.
40	F	W	Schiz.-Catat.	16 years	41	F	W	Schiz.-Catat.	15 years 10 mos.
34	F	NW	Schiz.-Heb.	12 years 6 mos.	43	F	NW	Schiz.-Heb.	11 years 9 mos.
39	F	W	Schiz.-Heb.	8 years	34	F	W	Schiz.-Heb.	7 years 9 mos.
49	F	W	Schiz.-Heb.	16 years 3 mos.	47	F	W	Schiz.-Heb.	16 years
48	F	W	Schiz.-Par.	6 years 2 mos.	47	F	W	Schiz.-Par.	6 years 2 mos.
39	F	W	Manic-Dep., Dep. Type	7 years 8 mos.	33	F	W	Manic-Dep., Dep. Type	7 years 8 mos.
33	F	W	Schiz.-Catat.	5 years 7 mos.	42	F	W	Schiz.-Catat.	5 years 10 mos.
27	F	W	Schiz.-Par.	1 year 2 mos.	25	F	W	Schiz.-Par.	1 year 2 mos.
43	F	W	Schiz.-Par.	8 years 10 mos.	44	F	W	Schiz.-Par.	9 years 3 mos.
33	F	NW	Schiz.-Par.	2 years 9 mos.	33	F	NW	Schiz.-Par.	2 years 6 mos.
53	F	W	Schiz.-Par.	3 years	50	F	W	Schiz.-Par.	2 years 10 mos.
32	F	W	Schiz.-Heb.	13 years 3 mos.	35	F	W	Schiz.-Heb.	13 years 9 mos.
48	F	W	Schiz.-Par.	4 years 10 mos.	54	F	W	Schiz.-Par.	4 years 10 mos.
49	F	W	Manic-Dep., Manic Type	9 years	57	F	W	Manic-Dep., Manic Type	9 years 5 mos.
39	M	W	Schiz.-Par.	10 mos.	35	M	W	Schiz.-Par.	7 mos.
36	F	W	Schiz.-Par.	3 years 1 mo.	38	F	W	Schiz.-Par.	3 years
22	F	W	Schiz.-Mixed	2 years 2 mos.	22	F	W	Schiz.-Mixed	2 years 2 mos.
25	F	W	Schiz.-Heb.	7 years 3 mos.	29	F	W	Schiz.-Heb.	7 years 2 mos.

and 5 per cent as worse. Considering that the average length of hospitalization for these patients was over seven years, and that other therapies had failed, this seems to indicate significant improvement in terms of clinical impression.

Malamud-Sands Psychiatric Rating Scale

The Malamud-Sands scale is composed of 22 functions, including mental as well as behavioral aspects of psychopathology. The ratings were made several days prior to treatment and from five days to two weeks after psychosurgery, representing a consensus of ward physicians, nurses and attendants. While ratings at longer intervals would have been desirable, the needs of the patients in getting them out of the hospital were given priority, preventing more ratings being made. This scale is constructed in terms of a pre-psychotic "baseline" and deviations therefrom in an outwardly and inwardly direction along six-point continuua. Since a variety of personnel from the two hospitals made the evaluations, the criteria for improvement for each function of the scale was established in gross form and empirically defined as follows: Improvement was scored when a pathological-rating on the pre-treatment evaluation returned to a baseline-rating on the post-treatment appraisal; Unimprovement was counted when a post-treatment rating remained on the same side of the baseline, or moved from one side of the baseline to the other; Worse was tabulated when a post-treatment rating moved out from a pre-treatment baseline rating. Those functions having a baseline rating before and after treatment were excluded as irrelevant for the purpose of this study. Chi-square tests of significance between the lobotomy and control groups for each of the scale-functions were computed, using Yates' correction for continuity. The degree of significant difference was then tested by corrected contingency coefficients.

Significant improvement in the lobotomized group over the matched control subjects was found in half of the 22 functions of this scale. In order of importance, significant improvement for the transorbital lobotomy patients was found in: insight, attention, thought processes, affect, perception, associations, work, socialization, awareness, subjective reorganization, and memory (Table 2). No difference between the two groups was found for the functions of feeling, mood, speech, sleep, sexual behavior, eating habits, hostility reactions, responsivity, mimetic expression, motor activity, and appearance. It is of interest to note that differences in gross improvement between the two groups of cases occurred more in the psychiatric, mental functions and less in the behavioral components of the rating scale. Apparently either transorbital lobotomy affected the mental processes of these patients more than the behavioral functions, or the Malamud rating scale more sensitively measured these changes than the more over action-components of the patients in the wards. Figure 1

TABLE 2

*Gross Improvement in Eleven Psychiatric Functions Found Significantly Different Between Transorbital Lobotomy and Control Patients.**

Function	Group	Improved		Unimproved		Totals	
		N	%	N	%	N	%
Insight [a]	Lobotomy	17	81	4	19	21	50
	Control	3	14	18	86	21	50
Attention [b]	Lobotomy	14	67	7	33	21	50
	Control	1	5	20	95	21	50
Thought Processes [c]	Lobotomy	19	53	9	47	19	50
	Control	0	0	10	100	19	50
Affect [d]	Lobotomy	10	59	7	41	17	50
	Control	1	6	16	94	17	50
Perception [e]	Lobotomy	11	61	7	39	18	50
	Control	2	11	16	89	18	50
Association [f]	Lobotomy	10	53	9	47	19	50
	Control	2	11	17	89	19	50
Work [g]	Lobotomy	14	67	7	33	21	50
	Control	5	24	16	76	21	50
Socialization [h]	Lobotomy	11	55	9	45	20	50
	Control	3	15	17	85	20	50
Awareness [i]	Lobotomy	10	48	11	52	21	50
	Control	2	10	19	90	21	50
Subjective Reorganization [j]	Lobotomy	8	42	11	58	19	50
	Control	1	5	18	95	19	50
Memory [k]	Lobotomy	13	62	8	38	21	50
	Control	2	10	19	90	21	50

a Chi-square=16.12; $p<.001$; C=.74
b Chi-square=14.94; $p<.001$; C=.72
c Chi-square=11.00; $p<.001$; C=.67
d Chi-square=8.60; $p<.01$; C=.64
e Chi-square=7.70; $p<.01$; C=.59
f Chi-square=5.96; $p<.02$; C=.52
g Chi-square=6.14; $p<.02$; C=.51
h Chi-square=5.38; $p<.05$; C=.49
i Chi-square=5.72; $p<.02$; C=.49
j Chi-square=5.24; $p<.05$; C=.49
k Chi-square=5.18; $p<.05$; C=.47

* Yates' correction for continuity was used in all chi-square computations.

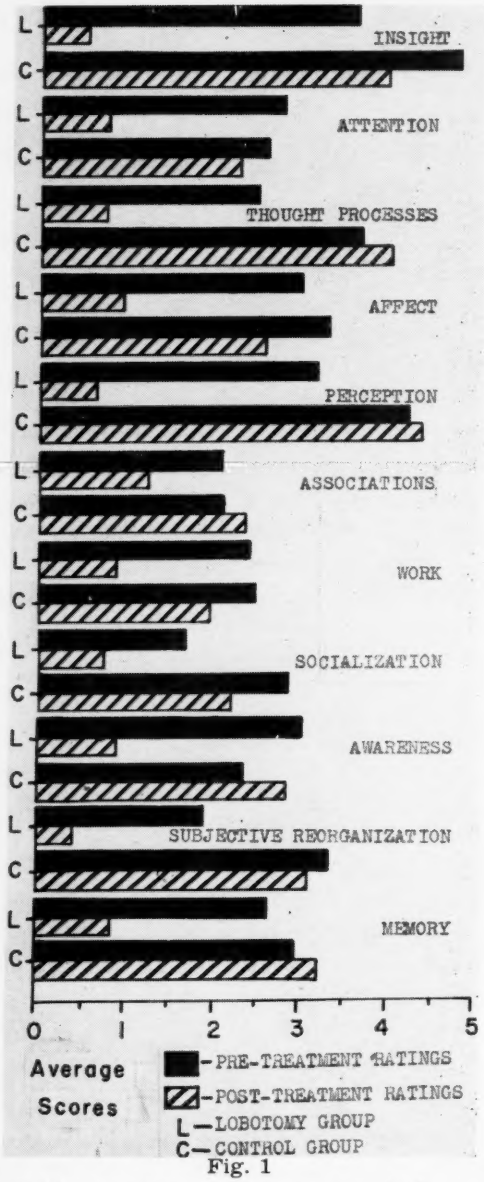


Fig. 1

shows the average rating scores before and after treatment for the lobotomized and control groups for the eleven significantly different functions. An analysis of each of these functions in the order of their degree of significance between the transorbital lobotomy and control groups of patients follows:

Insight: The majority of both psychosurgical and control patients exhibited more of what Malamud termed "centrifugal," or outwardly directed activities and orientations, of this function than "centripetal" pathology, a withdrawing from contact with the outside and a turning inward of actions and orientations.[9] The majority of the patients prior to lobotomy negated their problems or held others to blame for their mental difficulties. This condition was somewhat more extreme for the control patients. After psychosurgery, these patients exhibited no inwardly oriented pathology and a striking reduction in the outwardly directed pathological insight. Little alteration in this function occurred for the control group. Figure 2 illustrates the pre- and post-treatment ratings of the lobotomized and control patients.

Attention: For both the psychosurgical and control groups, this function was generally more inwardly than outwardly directed. Attention was mostly disparative and completely withdrawn, this being somewhat more marked for the control than for the lobotomy cases. Figure 3 shows that a reduction in both inwardly and outwardly directed attention occurred for the lobotomized group while the little change that took place in this function for the control patients was a slight increase in outwardly directed (more distractible) attention.

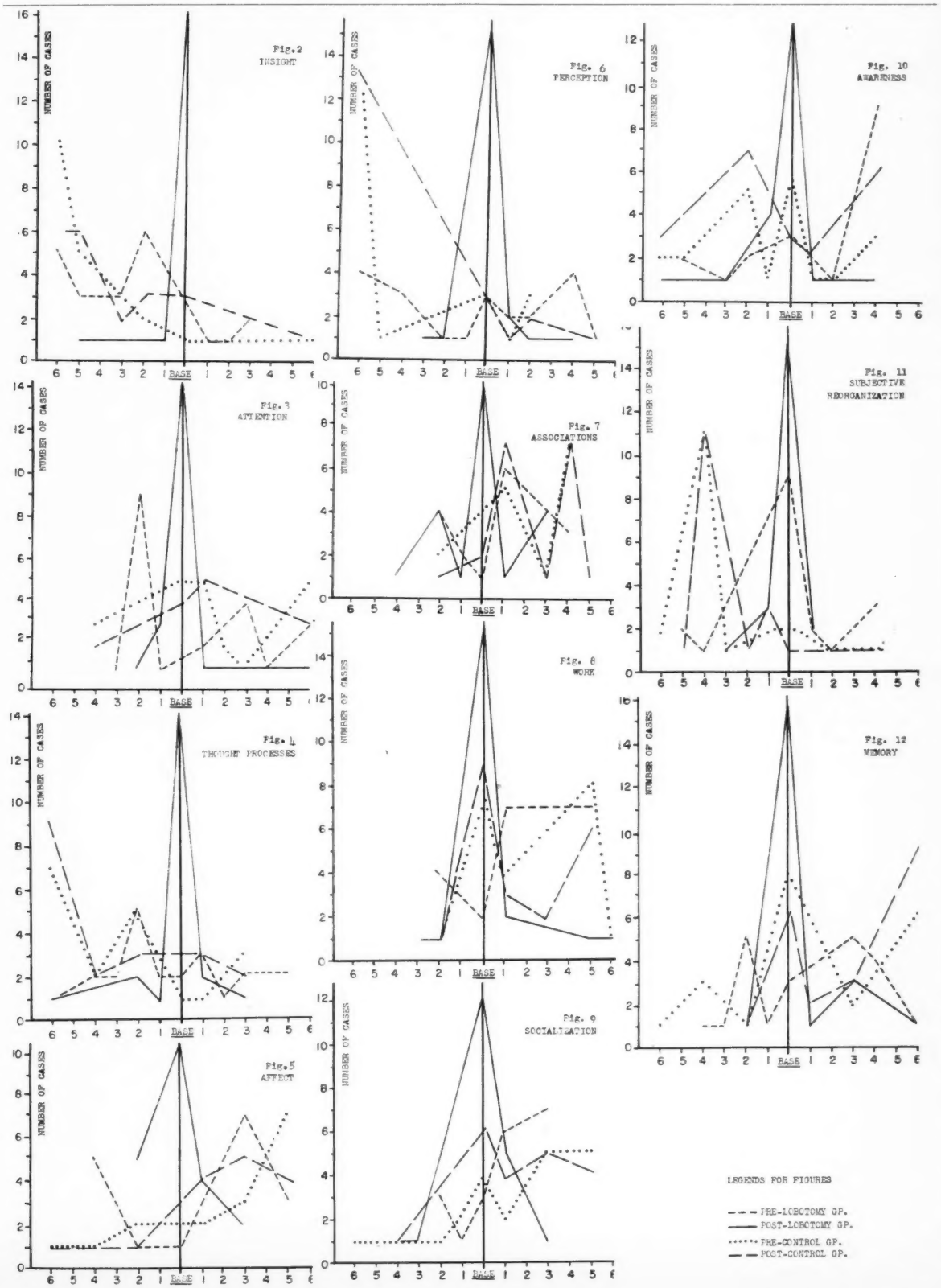
Thought Processes: Before transorbital lobotomy, these cases showed more fragmented and paralogical and alogical thought processes than obsessive doubt and hair-splitting, and rationalizing, although a third exhibited the latter orientation. Both sides of the baseline were considerably affected after transorbital lobotomy, showing a significant reduction in both extremes. The control patients also exhibited more outwardly than inwardly oriented thought processes, showing little or no change in the post-treatment rating period. These results are depicted in Figure 4.

Affect: Prior to treatment, both the transorbital lobotomy and control group showed more inwardly than outwardly directed pathology in this function, affect being more flat (rigid), bland and inadequate than labile and explosive. The post-treatment ratings indicated a significant reduction in pathological affect for the psychosurgical group, while little alteration in this function occurred for the control cases, as shown in Figure 5.

Perception: Pre-treatment ratings of the transorbital lobotomy patients were about equally divided in outwardly and inwardly directed perceptions while the control group was markedly outwardly hallucinating. Post-

treatment ratings of the psychosurgical group revealed a significant reduction in both pathological extremes, with more reduction in the outward direction than inward. Little change occurred in post-treatment ratings for the control subjects (Figure 6).

Associations: This function was rated to



be more centripetal than centrifugal for both the lobotomy and control groups prior to treatment, the extent of the pathology identical. Post-treatment ratings for the psychosurgical patients indicated a greater reduction in the inwardly directed pathology with little change in the outwardly oriented associations. A slight increase in inwardly directed pathology was noticed for the control cases (Figure 7).

Work: Work for both the lobotomy and control patients was more sporadic-ineffective and resistant than scattered, disorganized, and over-active before treatment. The ratings after treatment indicated a significant reduction in pathological extremes on both sides of the baseline for the transorbital lobotomy cases, while the control group demonstrated little or no change (Figure 8).

Socialization: The degree of pathology of this function was less for the psychosurgical group than for the control cases prior to treatment, although the direction was similar. Both groups indicated more isolated and shut-in social behavior on the hospital wards prior to treatment than out-reaching and meddlesome socialization. Post-treatment ratings indicated little change for the control group, while the lobotomized patients showed significant improvement in this function (Figure 9).

Awareness: The extent of pathology in this function was greater for the psychosurgical group before treatment than for the control cases. However, the direction of pathology was opposite for the two groups. Awareness for the lobotomy group was more cloudy (disoriented) and perplexed than splitting and confused before treatment while the opposite ratings were assessed to the control subjects. Following treatment, the ratings indicated more reduction in inwardly than outwardly directed awareness for the transorbital lobotomy patients while the control cases increased their pathological ratings more toward an inward direction (Figure 10).

Subjective Reorganization: Ratings made prior to treatment indicated a slightly more outwardly than inwardly directed pathology for the lobotomy group while the control patients indicated considerably more ideas of persecution and cosmic delusions (omnipotence) than somatic delusions. The degree of pathology was also greater for the control than for the lobotomy subjects. Post-treatment ratings indicated significant reduction in both types of pathology for the lobotomy cases while little alteration in the ratings occurred for the control group (Figure 11).

Memory: The extent of pathology of this function was very similar for both the groups before treatment, while the ratings following treatment indicated significant improvement for the lobotomy group and an increase in degree of pathology for the control cases. Pre-treatment ratings showed both study-groups to be more inwardly than outwardly oriented in memory. Post-treatment ratings indicated more reduction in inward than outward pathological memory functioning for the psychosurgical group, while the control patients showed an increase in inwardly-oriented memory pathology (Figure 12).

In summary, the results of transorbital lobotomy as indicated by the Malamud-Sands rating scale showed significant improvement in 11 of the 22 functions comprising this scale. While the lobotomy and control groups showed extreme pathology in both an inwardly and outwardly direction in all of the 11 significant functions prior to treatment, the psychosurgical cases exhibited more centripetal than centrifugal pathology than the control patients. No change in the direction of pathology occurred for the control group after treatment, while the transorbital lobotomy group showed a small decrease in inwardly directed functioning following psychosurgery (Table 3). These ratings were made independently by staff presonnel in two separate hospitals. Since only gross improvement, as indicated by a shift in a pathological rating to the baseline following treatment, was considered in the statistical analysis herein, we feel that this rating scale is a reasonably reliable indicator of the results of treatment. Consequently, the conclusion seems warranted that significant immediate improvement occurred in the transorbital lobotomy group more in certain mental functioning than behavior on the wards in contrast to a matched group receiving EST and ICT.

Wittenborn Rating Scale

This scale is composed of 55 items of behavior of the patient. These items have been factored into nine clusters or sub-scales: anxiety, conversion hysteria, manic, depressed, schizoid excitement, paranoid schizophrenia, paranoid condition, hebephrenic schizophrenia, and phobic compulsive. Standard scores ranging from one to ten have been computed for each of these sub-scales. This scale was administered before and after treatment to both the experimental and control subjects. In addition, this scale was administered by social caseworkers, familiar with the terminology used in the scale, in the homes of the patients before and after release from the hospital following treatment. Hospital ratings comprised the consensus of ward physicians, nurses and attendants while the caseworker sought the consensus of family members before making final judgment. Improvement was scored when a decrease in standard scores for each of the sub-scales occurred following treatment. However, no significant differences in any of the nine clusters was found between the psychosurgical and control patients after treatment. Neither was any significant difference found in the home-ratings before and after release from the hospital for those returning home during the 18-month follow-up study period.

Since the scale is concerned essentially with behavioral ratings, lack of significant findings between the two study-groups is consistent with the failure to find differences in most of the behaviorial functions of the Malamud-Sands scale. Apparently, either behavior of patients is not significantly affected by transorbital lobotomy or both rating scales are ineffective in determining any differences. We prefer the former explanation, since we are convinced that both rating scales, employed even in gross form, should be able to detect significant differences in the behavior of patients in both groups.

Release from Hospital

The rate of release from hospital is not always a reliable and valid index of the success or failure of treatment, since it reflects more of therapeutic and pathogenic elements in the patients' social situation than psychiatric status. Nevertheless, part of the complex of factors affecting release from hospital is the capacity of the patient to live outside. Among the factors involved in evaluating successful outcome of any treatment should be its influence on the patient's capacity to live outside of the hospital in addition to removing psychiatric disturbance. Lobotomy in general, and prefrontal in particular, has been criticized mostly for the risk it seemingly increases in depriving the patient of cerebral resources needed to survive in human society independently. Consequently, the effect of transorbital lobotomy upon the rate of release from hospital and to remain out was considered an important aspect of evaluating this mode of treatment.

Three-fourths of the lobotomized patients were released from hospital shortly after psychosurgery, while none of the matched control cases were released. A follow-up check 18 months later showed that 43 per cent were out of the hospital (19 per cent remaining out since their lobotomy, 24 per cent had been in earlier); 33 per cent were now in, but had been out during the year and a half period; and 24 per cent had never left the hospital. Two of the lobotomy patients had expired during this time, one year after psychosurgery outside of the hospital and the other 8 months after the operation in the hospital, both from causes other than due to psychosurgery. None of the control patients were released from hospital during this 18-month follow-up study period. Thus, a highly significant difference in release from hospital was obtained between the lobotomy and control cases, showing significantly more lobotomized patients leaving the hospital than the control subjects. (These results are presented in Table 3.)

This finding can be interpreted in at least three possible ways: 1. Transorbital lobotomy for these groups of patients improves the capacity to live outside of the hospital better than EST and ICT; 2. The administering of psychosurgery and stimulating new interest in the relatives and in psychotic patients who have been hospitalized for a long time improves the social climate for such

TABLE 3

Differential Release From Hospital of Transorbital Lobotomy and Control Patients

18 MONTHS AFTER TREATMENT: Patient-Group:	In Hospital: N	%	Out of Hosp.: N	%	Total: N	%
Lobotomy Group*	12	57	9	43	21	50
Control Group	21	100	0	0	21	50

In Hospital		Out					
Never Out		In		Has Been Out		Has Been In	Remain. Out
TRANSORBITAL LOBOTOMY AFTER 18 MONTHS:							
N	%	N	%	N	%	N	%
5	24	7	33	5	24	4	19

*Chi-square=9.06; p<.01; C=.60 (Yates correction used).

patients who may eventually be released from hospital and enables them to remain outside; 3. Renewed hope for these patients when they agree to the performance of the operation may induce a more permissive and custodial environment among family-members of the patient and take more positive action in helping the patient live in the home. Whether transorbital lobotomy improved the patients' social adaptability or stimulated the family of the patient to provide more therapeutic living conditions should he be released from hospital is still inconclusive. Nevertheless, in either case the patients administered this form of lobotomy were better able to leave and remain out of the hospital than a similar group of patients receiving other modes of therapy. Although beyond the scope of this paper, a more intensive analysis of the adjustment of these patients in the extra-hospital world is being conducted.

Summary and Conclusions

Two groups of psychotic patients in two different state hospitals were studied before and after treatment, and followed-up in and out of hospital for eighteen months. A group of 21 patients given transorbital lobotomy were matched on age, sex, color, diagnosis, and length of hospitalization with a group receiving EST and ICT in another state's hospital. Evaluation of both groups before and after treatment was made in terms of clinical impression, Malamud-Sands psychiatric rating scale, Wittenborn rating scale, and release from hospital. Significantly more improvement was found for the lobotomized group than for the control group in clinical impression, in eleven functions of the Malamud-Sands scale: insight, attention, thought processes, affect, perception, association, work, socialization, awareness, subjective reorganization, and memory, and in the amount of release from and remaining out of the hospital 18 months following psychosurgery. No significant differences were found in gross improvement for most of the behavioral functions of the Malamud-Sands scale (feeling, speech, sleep, sexual behavior, eating habits, hostility reactions, responsivity, mimetic expression motor activity, mood, and appearance), nor in the nine sub-scales of the Wittenborn scale (anxiety, conversion hysteria, manic, depressed, schiz. excitement, paranoid condition, paranoid schizophrenia, hebephrenic schizophrenia, and phobic-compulsion) between the lobotomy and non-lobotomized cases.

In terms of the measurements and indices used in this study, transorbital lobotomy was significantly more effective in relieving psychiatric disturbances and in enabling "backward" psychotic patients in a state hospital to be released from hospital than patients in a similar psychotic state receiving other somatic forms of treatment. In view of the poor prognosis of these patients and their long length of hospitalization, these results seem especially remarkable in favor of this mode of treatment for psychotic patients who are refractory to typical somatic therapies.

Acknowledgments are due Richard Neel of Rusk State Hospital and Joe Pearce of Austin State Hospital as well as the staffs of these two state hospitals for their assistance and cooperation in compiling the data.

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Subconvulsive Electrotherapy in Mental Disorders

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Electroconvulsive therapy is now recognized as a definite mode of treatment for many types of mental disorders. Since the physiological criteria which quiet the bizarre mental uproars are not yet fully understood due to the meagerness of knowledge pertaining to electrotherapy, a variety of procedures have arisen, and many electrical instruments have been introduced. Each manufacturer claims superiority for his particular machine. It is not definitely known, however, whether one machine stimulates or excites the brain better than another machine. In fact, there is no definite data on the specific brain mechanism whereby the amnesia, sleep and quietness are produced. Moreover, the longer one uses this form of therapy, the less convinced he becomes that even a convulsion is at all necessary for therapeutic results. My own experience, using mostly subconvulsive stimulation, has resulted in quieting the patient without the inherent and undesirable effects encountered in a convulsion, e.g. dislocations, fractures, excessive muscular contractions, lasting amnesia, etc.

In subconvulsive electrotherapy one aspect seems essential; namely, daily administration of electrical reaction for beneficial results. For subconvulsive treatment, only a 70 to 80 M.V. for 0.2 of a second are necessary. This produces mild muscular tension without giving rise to a convulsion. The patient soon regains wakefulness, is quieted without appreciable amnesia or any other side effects. In greatly disturbed patients, repetition of induction of the same current is necessary from 2 to 3 times within a few minutes when the patient usually quiets down.

Generally, I do not use intravenous sedation prior to the electrotherapy because of the possibility of apnea and therefore anoxia. The slight anxiety the patient may experience is not compensated for by the metabolic disorder it produces. In gravely and violently disturbed patients, intravenous sedation may have to be used.

Patients treated subconvulsively included the cyclothymias; namely, manic, manic depressive, presenile and senile melancholia, a variety of anxiety states and schizophrenia with behavioral disturbances. All of these were treated at the Los Angeles Neurological Institute. The greater number were given daily subconvulsive electrotreatments without intravenous sedation to obviate apnea and anoxia. The greatest number of these patients made as satisfactorily a recovery as those with convulsion.

The subconvulsive electrotherapy described here is not new. The purpose of these remarks is to encourage its trial by others, for greater ease of procedure and lesser hazard to the patient.

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Humoral Arousal Responses in Mental Disease

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Interest in the reactivity and particularly the presence or lack of autonomic responses in schizophrenia and different schizophrenic groups has waxed and waned in psychiatry. Some workers, however, have shown a consistent interest. Recent pharmacological development has again created a general interest in the neurophysiological activity of emotionally sick people.

Many have noted that certain schizophrenic patients do not show good peripheral autonomic responses clinically or experimentally.[1,2,3] It had also been demonstrated by Grinker and Serota[2] (1940) that schizophrenic patients also showed a lack of electroencephalographic responsiveness to injected adrenalin when compared to a group of normals and neurotics. Others[3,4] reported that clinical symptoms could be activated by intravenously administered adrenalin. At the time of these studies there was available only adrenalin containing both epinephrine and nor-epinephrine, these agents having no tthen been separated. More recently Dell, Bonvallet and Hiebel[5] showed in experimental animals that a small section of the reticular system is responsive to l-norepinephrine and that this area in animals responds to intravenous injection of the substance with arousal responses as shown by electroencephalographic tracing. Work by Diethelm and others[6] indicated that adrenergic substances occur in the blood of subjects under the emotional reactions of anxiety. In an effort to determine whether this substance was epinephrine or nor-epinephrine, Fleetwood,[7] by careful pharmacological experiment, demonstrated a substance in the blood of patients with anxiety reactions to be nor-epinephrine and not epinephrine-like.

The need to extend studies to other groups and to reevaluate the work done with the earlier adrnealin but now with the separate adrenergic agents seemed apparent. In this study patients with simple, hebephrenic or undifferentiated forms of schizophrenia, normals and neurotics were studied using l-norepinephrine in an attempt to determine the presence or absence of the arousal response in these groups. Blood pressure responses were also recorded in an attempt to correlate the central and peripheral responses.

Subject Material and Clinical Data:

The subjects studied consisted of 31 normotensive patients. These were divided into two groups; those who had no symptoms of schizophrenia and those subjects with a diagnosis of schizophrenia of either hebephrenic simple or undifferentiated type. The "normal group" consisted of 4 students and 9 patients from the psychiatric service of the Veterans Administration Hospital, Durham, N. C. The patient group complained of and were observed to have psychoneurotic illnesses characterized by chronic symptoms of anxiety and, to a lesser extent, manifestations of depression. The 18 schizophrenic patients were obtained from the psychiatric service of the V. A. Hospitals in Durham and Salisbury, N. C. Only those schizophrenic patients who showed (1) marked disturbance of affect with relative lack of affective responses, (2) disturbances in association, and (3) lack of paranoid ideation were included in the series. A history indicative of progressive behavioral and ideational disorganization was present in all cases. These criteria were used to select those patients who it was anticipated would most likely show poor autonomic responses. No patient had received somatic therapy within two years preceding this study. Some patients had never received any somatic therapy. None were on tranquilizing drugs; one had had a small dose of reserpine 28 days previously.

Clinical Data:

The mean age of the normal group was 33 years with a range of 21 to 40. The mean age of the schizophrenic group was 34 years with a range of 22 to 60 years. The mean duration of illness of the group of patients with anxiety symptoms was four years with a range of six months to 11 years. The mean duration of illness for those subjects with

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schizophrenia was 11 years with a range of nine months to 36 years. Only one of this latter group had been sick less than two years.

Method:

Electroencephalograms were obtained with silver-silver chloride electrodes applied to frontal, central, parietal, occipital, temporal and vertex regions using collodion or bentonite paste.

The l-nor-epinephrine used in the study was commercially available Levophed® and was mixed with normal saline to a dilution of 32 mce per cc. Eighteen to 32 mce was then injected into the medical antibrachial cutaneous vein over a period of five seconds. The termination of the injection was marked on the EEG recording. Blood pressures were obtained by the cuff and auscultatory method with the arm and heart level. Resting blood pressures were taken until this had stabilized and each 15 seconds after the termination of the injection. These blood pressures as well were recorded on the EEG tracing. The mean arterial pressure was then calculated from these values.

Results:

In analyzing the EEG's the following criteria were used to establish the presence of arousal:

1. No response was used unless this occurred between 20 and 30 seconds following the injection of the drug.
2. The response must be characterized by a 50% to 75% reduction in voltage of the record with a clear increase in the frequency. The responses obtained had to be similar to those obtained to single light flashes of sound stimuli during a control period.

The occurrence of arousal in the normal and neurotic group (figure 1) when compared with the schizophrenic group (figure 2) was significantly greater. Nine of the primary group showed arousal, whereas only four of the schizophrenics showed any evidence of a change in the record. There was also a significant difference in the duration of the response. The duration in the normal and neurotic group was 3.8 seconds and only 1.5 seconds in the schizophrenics. Figure 1 shows arousal, characteristic of the neurotic as occurring in about 23 seconds. This is particularly clear in lead C_4 - P_4, C_3 - P_3 and P_3 - O_1. Figure 2, in contrast, shows the lack

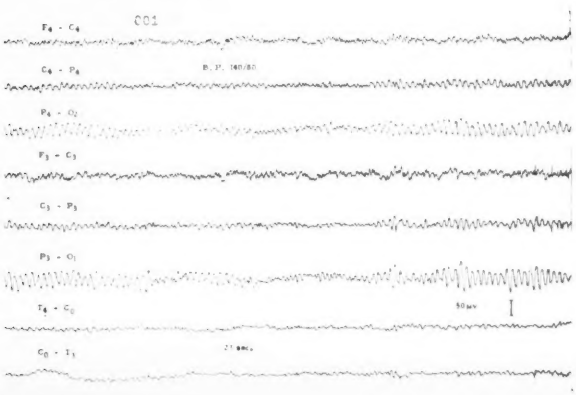

Fig. 1

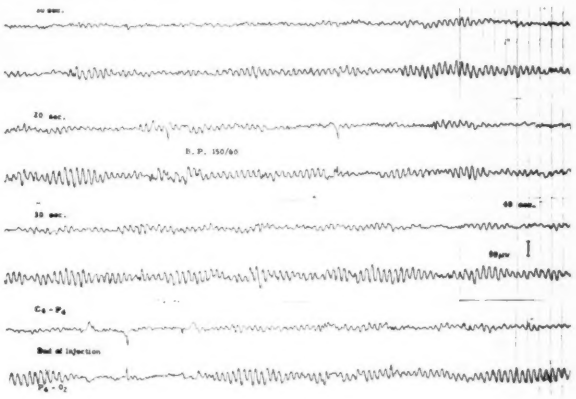

Fig. 2

of arousal that is characteristic of the schizophrenic group.

Blood Pressure Responses:

The mean arterial blood pressures in the two groups showed no significant differences.

Clinical Observations Following Injection of Nor-epinephrine:

Following the introduction of the needle brief arousal was observed. After the record had stabilized the injection was made. This was followed in 10 to 15 seconds by a respiratory gasp — one to two seconds elapsed and arousal was then observed accompanied by a subjective feeling of anxiety in some of the normals and patients with anxiety neuroses. Next there occurred a blood pressure response accompanied by a pounding headache and occasionally by a subjective feeling of throbbing in the extremities. None of the schizophrenic group complained of subjective feelings of anxiety. Some patients in the schizophrenic group

felt that they could breathe better after the injection.

Discussion:

The report of Grinker and Serota[2] demonstrating difference in arousal responses in normals and in schizophrenics to circulating adrenalin is confirmed in part by this study. Although our technique was varied markedly from thae used by Grinker, it seems fair to state that there appears a decided insensitivity of central activity to the humoral agent l-nor-epinephrine in schizophrenia, The mechanism by which this phenomena occurs is not clear. Bonvallet, Dell and Hiebel[5] felt that the responses seen in animals were due to the effect of the agent on the reticular system, but Nakao et al.[8] in a recent report have demonstrated a similar response originating in the carotid sinus, mediated htrough the reticular system.

In some recent work[9] micro injection of l-nor-epinephrine by another worker into a very small portion of the reticular region has resulted in cortical arousal similar to that seen with intravenous injection into the same animal. This response also occurred on occasion following the injection of neutral substances into the same area. This work would indicate the possibility of an entirely central mechanism being responsible for cortical arousal. However, since this issue has still not been clarified, it may be said that a lack of central responsiveness as seen in the schizophrenic is further indicaiton that central as well as peripheral autonomic mechanisms are involved. This is in keeping with the postulates of Dennis Hill[10] using another approach to the study of the central activity in schizophrenia.

The similarity of blood pressure responses in the two groups cannot easily be explained. Previous authors have demonstrated a very significant difference in the blood pressure responses to l-epinephrine: however, the drug was given intramuscularly and in larger doses than in this study. It is also important that there appears to be no reports in the literature concerning the blood pressure response to l-nor-epinephrine on psychiatric patients, and that comments made concerning its role in mental disease have, as Funkenstein[11] stated and noted by Marrazzi,[12] involved much reasoning by analogy.

In summary this study has demonstrated a significant depression in the EEG responses to intravenous nor-epinephrine in schizophrenics, and little difference in the blood pressure responses of a group of normal and neurotic patients when compared with a group of schizophrenic patients.

Non-schizophrenic patients do not universally show arousal responses to nor-epinephrine. Further work concerning the role of l-epinephrine in eliciting these responses is projected.

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The Use of Reserpine (Serpasil) in Mentally Ill Epileptics

CLYDE BROOKS, M.D.

When reserpine (Serpasil®) was first considered for use in our cases early in 1954, the question arose as to whether it could safely be used in convulsive mentally ill patients. At that time there was no published work on the effects of reserpine in such patients, so far as the author could find. Personal communication from one observer indicated that the drug was contraindicated in epileptics, because it increased the incidence of seizures.

However, in convulsive mental patients there is great need for the tranquilizing, stabilizing effects of reserpine because the mere control of the seizures by Dilantin, phenobarbital or other anticonvulsant drugs leaves the patient with his moodiness, overactivity and personality changes unimproved. Since our work was started, several publications reporting the use of reserpine in convulsive mental cases have appeared.

Lambros[3] found that nearly all his epileptic mental cases improved with reserpine; the patients showed a more constant and predictable personality. In about one-fourth of his cases, the amount of anticonvulsant medication could be reduced without any increase in convulsive seizures while reserpine was being taken.

Zimmerman and Burgemeister[4] found no significant change in the weekly incidence of attacks for the group as a whole, but 31 cases showed reduction of frequency of attacks; 30 cases showed no change; 39 cases showed some increase in the frequency of attacks during reserpine therapy.

Carter[5] found lessening of tension and apprehension and in many cases lessening of severity of the seizures, with shortening of the recovery periods. In psychogenic epilepsy he observed marked improvement, many cases showing complete cessation of seizures. This author found no contraindication against the adjunctive use of reserpine in epileptics.

Barsa and Kline[6] found reserpine less effective in psychotic patients with convulsive disorders than in psychotics without convulsive seizures. They also reported an increased incidence of convulsive seizures during the first six weeks of reserpine therapy.

Our plan of study was to observe a group of epileptic, mentally ill patients by giving to each only the required daily dosage of anticonvulsant medication for a control period. Next we follow the same group of patients for another period while giving them the same dosages of anticonvulsant medication with the addition of individually adequate doses of reserpine.

In some instances the control period was one month and the reserpine therapy period was also one month. However, during the major part of the study the control periods were 2, 3 or 4 months, while the reserpine therapy periods were 2, 4 or 5 months, with a final period which has run 8 months. As our data are reported, the total time covered is two years and eight months, and the study is being continued.

At the outset 57 patients were selected; later 63 more patients were added, making a total of 120 cases.

Most of the patients received daily three capsules of Dilantin (each capsule 0.1 Gm.), while a few received four daily. Some received phenobarbital (½ to 1½ gr.) in addition. With few exceptions the dosage established for each patient was continued unchanged during the control periods and during the reserpine therapy periods.

The attached tabulation shows the total number of seizures for 211 patients per month of the entire study and the daily dosage given to each patient during the periods of its inclusion was 2, 4 or 5 mg. of Serpasil.

Analysis of the figures shows that the over-all average of incidence of seizures during the control periods is significantly greater than that during the reserpine therapy periods, as follows: in control periods, 3.72 seizures per month; in the reserpine therapy periods, 2.5 seizures per month. These data cover a rather long period of time (two years and eight months), and a fairly large group of cases (120); the de-

From Alabama State Hospitals, Tuscaloosa, Ala.

crease in seizures by approximately one-third is regarded as significant.

In this study the side effects of reserpine have not been dangerous nor seriously troublesome; for most patients, with the dosage employed, the side effects were negligible. A few patients, especially in the early phases of the study, showed moderate slowing of the pulse rate and moderate lowering of blood pressure with some lassitude or listlessness. When the manifestations were too pronounced the reserpine was discontinued temporarily or the analeptic drug methylphenidate (Ritalin®) was administered.

Other side effects (more often seen in non-convulsive patients who received larger doses of reserpine) such as stuffiness of the nose, Parkinson-like symptoms (poker-face, trembling hands and arms), usually occurred in early phases of reserpine therapy. These stopped promptly when the drug was temporarily discontinued or methylphenidate was administered. In all cases, convulsive or nonconvulsive, there were no troublesome blood changes nor hepatic disorders. In review, there were few side effects and usually these were mild, only infrequently requiring temporary discontinuance of the reserpine or administration of Ritalin.

Our conclusion is that with the doses used in the present study reserpine therapy is safe and effective for epileptic mentally ill patients. The negativistic, uncooperative, restless, agitated, assaultive, combative, hostile patients became more quiet, cooperative, affable and friendly. Those who previously refused to talk to other patients or to attendants began to talk; in those not previously mute the talk was more relevant. Patients who had been moody, morose, and refused to take part in any ward activities, who never looked at television or motion picture shows, who could not be trusted out of their rooms, changed and now are participating in activities, going to church, to baseball games, on bus rides, swimming and now help with housekeeping work on the wards. Some work in dining rooms, some in the laundry. Some have joined clubs, and others work in the occupational therapy department. Most of the patients taking reserpine eat better and gain weight. Many of them, when they are improved, ask to be sent home, and many have been furloughed and are well adjusted outside the hospital.

TABLE I

Total number of patients	Total number of patient-months during control periods (no Serpasil)	Total number of patient-months during Serpasil treatment.	Average number of convulsions per patient per month during control periods (no Serpasil)	Average number of convulsions per patient per month during Serpasil treatment
120	717	770	3.72	2.5

Summary

In a study covering 2 years and 8 months, including 120 cases, reserpine in doses from 2 to 5 mg. per day (with standard anticonvulsant medication) reduced the incidence of convulsive seizures in mentally ill epileptics by about 33%, in addition to ameliorating the signs and symptoms of their disturbed state.

Reserpine is a safe and effective agent in the treatment of mentally ill epileptics.

Author's Note: Serpasil and Ritalin used in this study were supplied by Ciba Pharmaceutical Products, Inc.

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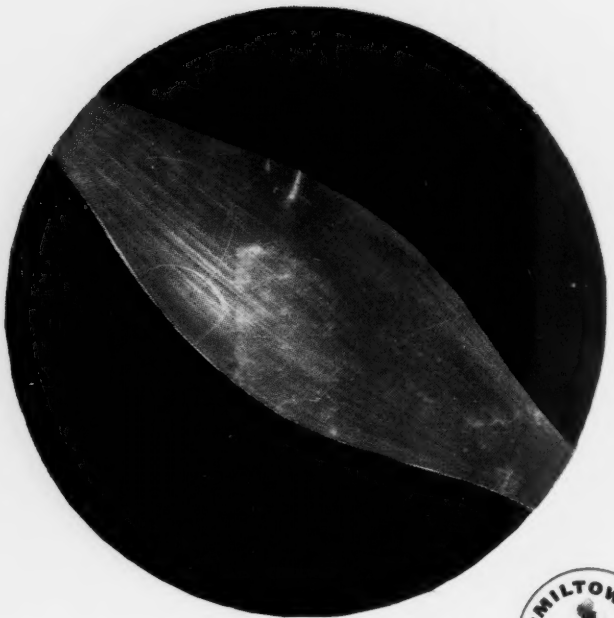

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